What is claimed is:

1. A computer-assisted method for generating predicted binding targets of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in the selected molecule;

(b) determining, using the processor, for each atom in the selected molecule, a predicted Gibbs free energy of binding of the atom to an ideal ligand for the atom;

(c) generating, using the processor, a three-dimensional prediction model of binding targets in the selected molecule by generating, using the three-dimensional coordinates of each of the atoms in the selected molecule, a model of the atoms in the selected molecule and mapping onto each atom depicted in the model the corresponding determined predicted Gibbs free energy of binding; and

(d) outputting, to the output device, the generated three-dimensional prediction model of binding targets.

2. A computer-assisted method for predicting the binding affinity of a selected ligand for binding to a selected binding site of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in a selected compound;

(c) generating, using the processor, a model of the selected compound bound to the selected binding site;

(d) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected compound when the selected compound is bound to the selected binding site; and

(e) determining, using the processor, a predicted binding affinity of the energy minimized selected compound for the selected binding site.

3. A computer-assisted method for building a model of an ideal ligand for binding to a selected binding site of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in the selected binding site of the selected molecule;

(b) determining, using the processor, the identity and location of a set of ligand atoms that are energetically complementary to each of the atoms in the selected binding site of the selected molecule based on global optimization of the Gibbs energy of binding of each of the ligand atoms in the set of ligand atoms;

(c) generating, using the processor, a three-dimensional model of the set of ligand atoms bound to the selected binding site;

(d) outputting, to the output device, the three-dimensional model of the set of ligand atoms bound to the selected binding site.

4. A computer-assisted method for ranking each ligand in a set of selected ligands by its predicted binding affinities for binding to a selected binding site of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including, the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) determining the predicted binding affinity of each ligand in the set of ligands to the selected binding site of the selected molecule by:

(i) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in the selected compound;

(ii) generating, using the processor, a model of the selected compound bound to the selected binding site;

(iii) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected compound when the selected compound is bound to the selected binding site; and

(iv) determining, using the processor, a predicted binding affinity of the energy minimized selected compound for the selected binding site; and

(b) ranking each ligand according to its determined predicted binding affinity.

5. A computer-assisted method for generating predicted binding targets on a internal, non-solvent exposed surface of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in a selected partially unfolded state of the selected molecule, the selected partially folded state including a folded portion and an unfolded portion;

(b) determining, using the processor, for each atom in the folded portion of the selected partially unfolded state of the selected molecule, a predicted Gibbs free energy of binding of the atom to the ideal ligand for the atom;

(c) generating, using the processor, a three-dimensional prediction model of binding targets in the folded portion of the selected partially unfolded state of the selected molecule by generating, using the three-dimensional coordinates of each of the atoms in the folded portion of the selected partially unfolded state of the selected molecule, a model of the atoms in the folded portion of the selected partially unfolded state of the selected molecule and mapping onto each atom depicted in the model the corresponding determined predicted Gibbs free energy of binding; and

(d) outputting, to the output device, the generated three-dimensional prediction model of binding targets.

6. A computer-assisted method for predicting the binding affinity of a selected peptide ligand for binding to a selected binding site of a selected molecule, using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data including the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) inputting into the programmed computer, through the input device, data including, the identity and three-dimensional coordinates of each of the atoms in a selected dipeptide;

(c) generating, using the processor, a model of the selected dipeptide bound to the selected binding site;

(d) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected dipeptide when the selected dipeptide is bound to the selected binding site; and

(e) determining, using the processor, a predicted binding affinity of the energy minimized dipeptide for the selected binding site.

7. The method of claim 6, further including:

repeating steps (a) - (e) for a plurality of selected dipeptides and identifying as a lead dipeptide the selected dipeptide having the highest determined binding affinity.

8. The method of claim 2, further including:

(f) selecting a first polypeptide of three or more amino acids, the polypeptide including the dipeptide;

(g) generating, using the processor, a model of the selected first polypeptide bound to the selected binding site;

(h) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected first polypeptide when the selected first polypeptide is bound to the selected binding site; and

(i) determining, using the processor, a predicted binding affinity of the energy minimized first polypeptide for the selected binding site.

9. The method of claim 8, further including:

(j) selecting a second polypeptide including the first polypeptide;

(k) generating, using the processor, a model of the selected second polypeptide bound to the selected binding site;

(l) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected second polypeptide when the second selected polypeptide is bound to the selected binding site; and

(m) determining, using the processor, a predicted binding affinity of the energy minimized second polypeptide for the selected binding site.

10. The method of claim 8, further including:

(j) selecting a variant of the selected polypeptide;

(k) generating, using the processor, a model of the selected variant polypeptide bound to the selected binding site;

(l) determining, using the processor, the three-dimensional coordinates of an energy minimized structure of the selected variant polypeptide when the selected variant polypeptide is bound to the selected binding site; and

(m) determining, using the processor, a predicted binding affinity of the energy minimized selected variant polypeptide for the selected binding site.

11. The method of claim 5 wherein the selected partially unfolded state is the partially unfolded state having the lowest Gibbs energy of any potential partially unfolded state of the selected molecule.

12. A computer program, residing on a computer-readable medium, for generating predicted binding targets of a selected molecule, the computer program including instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in the selected molecule;

(b) determine, for each atom in the selected molecule, a predicted Gibbs free energy of binding of the atom to an ideal ligand for the atom;

(c) generate a three-dimensional prediction model of binding targets in the selected molecule by generating, using the three-dimensional coordinates of each of the atoms in the selected molecule, a model of the atoms in the selected molecule and mapping onto each atom depicted in the model the corresponding determined predicted Gibbs free energy of binding; and

(d) output the generated three-dimensional prediction model of binding targets.

13. A computer program, residing on a computer-readable medium, for predicting the binding affinity of a selected ligand for binding to a selected binding site of a selected molecule, the computer program including instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) receive data including the identity and three-dimensional coordinates of each of the atoms in a selected compound;

(c) generate a model of the selected compound bound to the selected binding site;

(d) determine the three-dimensional coordinates of an energy minimized structure of the selected compound when the selected compound is bound to the selected binding site; and

(e) determine a predicted binding affinity of the energy minimized selected compound for the selected binding site.

14. A computer program, residing on a computer-readable medium, for building a model of an ideal ligand for binding to a selected binding site of a selected molecule, the computer program including instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in the selected binding site of the selected molecule;

(b) determine the identity and location of a set of ligand atoms that are energetically complementary to each of the atoms in the selected binding site of the selected molecule based on global optimization of the Gibbs energy of binding of each of the ligand atoms in the set of ligand atoms;

(c) generate a three-dimensional model of the set of ligand atoms bound to the selected binding site; and

(d) output the three-dimensional model of the set of ligand atoms bound to the

selected binding site.

15. A computer program, residing on a computer-readable medium, for ranking each ligand in a set of selected ligands by its predicted binding affinities for binding to a selected binding site of a selected molecule, the computer program including instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) determine the predicted binding affinity of each ligand in the set of ligands to the selected binding site of the selected molecule by:

(i) receiving data including the identity and three-dimensional coordinates of each of the atoms in the selected compound;

(ii) generating a model of the selected compound bound to the selected binding site;

(iii) determining the three-dimensional coordinates of an energy minimized structure of the selected compound when the selected compound is bound to the selected binding site; and

(iv) determining a predicted binding affinity of the energy minimized selected compound for the selected binding site;

(b) rank each ligand according to its determined predicted binding affinity.

16. A computer program, residing on a computer-readable medium, for generating predicted binding targets on a internal, non-solvent exposed surface of a selected molecule, the computer program including instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in a selected partially unfolded state of the selected molecule, the selected partially unfolded state including a folded portion and an unfolded portion;

(b) determine, for each atom in the folded portion of the selected partially unfolded state of the selected molecule, a predicted Gibbs free energy of binding of the atom to the ideal ligand for the atom;

(c) generate a three-dimensional prediction model of binding targets in the folded portion of the selected partially unfolded state of the selected molecule by generating, using the three-dimensional coordinates of each of the atoms in the folded portion of the selected partially unfolded state of the selected molecule, a model of the atoms in the folded portion of the selected partially unfolded state of the selected molecule and mapping onto each atom depicted in the model the corresponding determined predicted Gibbs free energy of binding; and

(d) output the generated three-dimensional prediction model of binding targets.

17. A computer program, residing on a computer-readable medium, for predicting the binding affinity of a selected peptide ligand for binding to a selected binding site of a selected molecule, the computer program comprising instructions for causing a computer to:

(a) receive data including the identity and three-dimensional coordinates of each of the atoms in a selected binding site of a selected molecule;

(b) receive data including, the identity and three-dimensional coordinates of each of the atoms in a selected dipeptide;

(c) generate a model of the selected dipeptide bound to the selected binding site;

(d) determine the three-dimensional coordinates of an energy minimized structure of the selected dipeptide when the selected dipeptide is bound to the selected binding site; and

(e) determine a predicted binding affinity of the energy minimized dipeptide for the selected binding site.